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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WANG, SHENGJUN	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/737,544	PEPYS, MARK B.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 39-56* is/are pending in the application.

4a) Of the above claim(s) *39 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 and 41-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/18/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted May 18, 2004 is acknowledged.

Claim Rejections 35 U.S.C. 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-9, 16-19, 39-41, 44-46, 49, 55, and 56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds as defined in claim 10, does not reasonably provide enablement for any other compounds defined as "capable of inhibiting the binding of C-creative protein to an autologous or extrinsic ligand thereof." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ 2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

The claim recites the employment of compounds "capable of inhibiting the binding of C-creative protein to an autologous or extrinsic ligand thereof." Applicants fail to provide information allowing skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of such compounds are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. Applicants define the compounds by their function instead of their structure, and provide no information as to the structural-activity relation ship. A person of ordinary skill in the art would have been required to perform undue experimentation to use claimed invention, particularly, to identify those compounds within claimed scope. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed: the vice of a functional claim exists not only when a claims is wholly functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty. Functional language at the point of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does little more than outline[e] goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate. Applicants

functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first or second paragraph. Claims employing functional language at the point of novelty, such as Applicants□, neither provide those elements required to practice the inventions, nor inform the public during the life of the patent of the limits of the monopoly asserted *General Electric Company v. Wabash Appliance Corporation et* supra, at 468.

The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed of physiological activity. The instant claims read on all compounds "capable of inhibiting the binding of C-creative protein to an autologous or extrinsic ligand thereof," necessitating an exhaustive search for the embodiments suitable to practice the claimed invention, absent undue experimentation.

Claim Rejections 35 U.S.C.§ 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-25 and 42-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhakdi et al. (IDS) and Kito, in further view of Yedgar et al. (US 5,064,817) and Wissner et al. (US 4,640,913).

5. Bhakdi et al. and Kito teaches that phosphorylcholine are useful for inhibiting the binding of CRP to LDL, wherein the binding of CRP to LDL is known to be a factor of atherosclerosis. See the abstracts.

6. The primary references do not teach expressly the employment of hexadecyl phosphorylcholine for treating atherosclerosis.

7. However, Yedgar et al. teaches that various phosphorylcholine derivatives are known to be useful for treating pathological conditions including atherosclerosis. See, particularly, column 13, lines 22-38, and the claims. Wissner et al. teaches various phosphorylcholine derivatives are useful for treating hypertension, an underline etiology of atherosclerosis. See, particularly, the abstract, column 1, lines 19-26, and the claims.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis.

A person of ordinary skill in the art would have been motivated to employ a phosphorylcholine compound, such as hexadecyl phosphorylcholine, for treating atherosclerosis because phosphorylcholine is known to inhibiting the binding of CRP to LDL is known to be a factor of atherosclerosis, suggesting the usefulness of phosphorylcholine for treating atherosclerosis, and a ester, or salt of an active therapeutical compound, would have considered, an equivalent of the active therapeutical compound. Further, phosphorylcholine derivatives are generally known to be useful for treating atherosclerosis. Withr respect to the new claims added herein reciting stroke, note, a method known to be useful for treating the underline etiology of a

disorder would have been reasonably expected to be useful for treating or preventing the disorder.

Response to the Arguments

Initially, it is noted claim 48 was properly rejected since it read on the elected invention and species.

Applicants' amendments and remarks submitted May 18, 2004 have been fully considered, but are not persuasive for reasons discussed below.

Applicants traverse the rejections under 35 U.S.C. 112 based on that "detailed procedures for making and using the invention may not be necessary....," and 3-D structure of CRP is known in the art. Applicants allege there is no need of undue experimentation to find the proper CRP inhibitors as herein claimed. The arguments are not persuasive. While it is true that claimed subject matter need not be described in *haec verba* in the specification, it is also true that the application should describe the claimed invention so that one skilled in the art can recognize what is claimed. The mere functional limitation herein provide no way for one skilled in the art to recognize what compounds are encompassed in the claims except a try and error method, which would be an undue experimentation. It should be well understood, at the current level of skill in the art, one possess a 3-D structure of an enzyme would not be recognized as possess all inhibitors, or ligands of that enzymes. A structurally novel inhibitor or ligand of a known enzyme would normally acquire separate status in the art as separate inventive subject matter. In deed, U.S. Court of Appeals Federal Circuit recently state: "Even with the three-dimensional structures of enzymes...., it may even now not be within the ordinary skill in the art to predict

what compounds might bind to and inhibit them,...." In re University of Rochester v. G.D.Seale& Co. 69 USPQ2d1886(CAFC 2004).

8. Applicants traverse the rejections under 35 U.S.C. 103 over Bhakdi et al. (IDS) and Kito, in further view of Yedgar et al. (US 5,064,817) and Wissner et al. (US 4,640,913) on the ground of alleged common knowledge of the skilled in the art. Particularly, Applicants cited Kilpatrick and Volanakis (1991), and Steel and Witehead (1994), both were published much earlier than Bhakdi references (1999), and earlier than or about the same time as Kito references (1993). The traverse is not persuasive. Particularly, at the time the claimed invention was made, skilled artisan would have possessed the knowledge taught by Bhakdi and Kito. Further, there is no contrary between Kilpatrick and Volanakis (1991) and Steel and Whitehead (1994) and Bhakdi and Kito. Kilpatrick and Volanakis (1991) and Steel and Whitehead (1994) teach CRP is acute phase protein responding to infection and inflammation, Kilpatrick and Volanakis (1991) and Steel and Whitehead (1994) does not teach the long term effect of CRP. In similar situation, it is well understood that inflammation and elevated body temperature are a mechanism of a mammal for defending itself from infection. However, this will not make anti-inflammatory therapy unobvious.

9. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, the primary references teaches that phosphorylcholine are useful for inhibiting the binding of CRP to LDL, wherein the binding of CRP to LDL is known to be a factor of atherosclerosis. And the

secondary references teach that phosphorylcholine derivatives are known to beneficial in treating atherosclerosis. Take the cited references as a whole, it would have been obvious for one of ordinary skill in the art to employ phosphorylcholine derivatives for treating atherosclerosis (an in vivo process) and related disorders.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang, Ph.D. whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday-Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9302.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang

August 18, 2004